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EXAMINER

BASI, NIRMAL SINGH

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 01/15/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/462,416

Applicant(s)
Rehovot et al

Examiner
Nirmal S. Basi

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1646



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Dec 14, 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-37 is/are pending in the application.
- 4a) Of the above, claim(s) 16-31 and 37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15 and 32-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 20) ☐ Other: _____

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DETAILED ACTION

1. Amendments filed 4/13/00 (paper number 5), 4/26/00 (paper number 7), 4/24/01 (paper number 9) and Election filed 12/4/01 (paper number 11) have been entered.

Election/Restriction

2. Applicant's election with traverse of Group I (Claims 1-15 and 32-36), in Paper No. 11 (10/29/01), is acknowledged. The traversal is on the ground(s) that Fischer (AH) disclose a fusion protein product and the protein of reference AH does not anticipate the present claim 1 as the protein of Fischer is shorter in that it excludes the N-terminal Ig domain, as well as the C-terminal tether domain of IL-6R, the protein of Fischer cannot be glycosylated in a similar fashion to the glycosylation of naturally-occurring sIL-6R and IL-6, as it is expressed in yeast, the definition of "essentially all" as appearing in the specification does not comprehend the truncated IL-6R of Fischer, nor does the definition of "analogs" comprehend such a truncated IL-6R, further, the term "glycosylated in a similar fashion to the glycosylation of naturally-occurring sIL-6" does not read on the glycosylation which occurs when the proteins are expressed in yeast. Applicants arguments have been fully considered but not found persuasive. The specification does not disclose the glycosylation pattern of the fusion protein, what is considered a similar fashion of glycosylation or definition of an analog which would exclude the polypeptide of Fischer et al as prior art. The definition of "essentially all" also does not exclude the polypeptide of Fischer et al as prior art. Further claim 1 does not recite the presence of N-terminal Ig domain, as well as the C-terminal tether domain of IL-6R. An examination of the materially different,

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patentably distinct inventions in a single application would constitute a serious undue burden on the examiner.

The requirement is still deemed proper and is therefore made FINAL.

3. The drawings objected to because each Figure must described separately in the Brief

5 Description of the Drawings. Figure 1C has not been described in the Brief Description of the Drawings.

Appropriate correction is required.

4. The amendment filed 7/24/01 objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter
10 into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: "In Fig. 1A, the reverse primer is complementary to SEQ ID NO:9 and in Fig. 1B, the EcoR1 enzyme recognition site and the strand of the Il-6 cDNA sequence is presented as SEQ ID NO:10".

Applicant is required to cancel the new matter in the reply to this Office action.

Claim Rejection, 35 U.S.C. 112

5. Claims 1-15 and 32-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 1 is indefinite because “being glycosylated in a similar fashion to the glycosylation of naturally occurring sIL-6R and IL-6” has not been defined so as to allow metes and bounds of the claims to be determined. The glycosylation patterns of the naturally occurring sIL-6R and IL-6 have not been disclosed. Further it is not clear when a sIL-6R/IL-6 and analogs thereof are glycosylated in a similar fashion to the naturally occurring sIL-6R and IL-6, as compared to when they are not glycosylated in a similar fashion to the naturally occurring sIL-6R and IL-6, so as to allow the metes and bounds of the claim to be determined.

Claim 1 is indefinite because it is not clear what is essentially all of the naturally occurring form of sIL-6R and essentially all of the naturally occurring form of IL-6 so as to allow metes and bounds of the claims to be determined. It is not clear when a sIL-6R or IL-6 are essentially all of the naturally occurring form of sIL-6R or IL-6, respectively, as compared to when they are not essentially all of the naturally occurring form of sIL-6R or IL-6, respectively, so as to allow the metes and bounds of the claim to be determined.

Claims 1 is indefinite because it is not clear what is an analog of sIL-6R/IL-6 so as to allow the metes and bounds of the claim to be determined. The term “analog” carries no weight in terms of structure and function and encompasses numerous alterations and reads on unrelated proteins, therefore the metes and bounds of the claim cannot be determined. Further it is not clear when the glycosylation of an analog is considered in a similar fashion to the naturally occurring sIL-6R and IL-6.

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Claim 1 is indefinite because it is not clear what “biological activity” the “biologically active analogs thereof” possess so as to allow the metes and bounds of the claims to be considered.

5 Claims 2-5, 13, 14, 15 and 32-33 are indefinite for the use of “biologically active analogs”, and “analogs” for reasons given in the rejection of claim 1.

Claims 6 and 7 are indefinite because the SEQ ID NO: of sIL-6R and IL-6 containing Val-356 and Pro-29 are not disclosed. Further “positions 357-359” refer to amino acids of a particular polypeptide sequence, the SEQ ID NO: of the polypeptide is not disclosed. Similarly, in claim 8 protein containing the MET-212 and VAL-112 must be identified by SEQ ID NO:.

10 Claims 6 and 7 are indefinite because sIL-6R δ Val/IL-6 are not art accepted terms and without a corresponding SEQ ID NO: for the construct the metes and bounds of the claim cannot be determined.

15 Claim 9 is indefinite because it is not clear when the chimeric protein is in a “fully processed form”, so as to allow the metes and bounds of the claim to be determined. Specifically what defines when a protein is in a fully processed form.

Claim 12 and 13 are indefinite because it is not clear when a tumor is “highly malignant” so as to allow the metes and bounds of the claim to be determined. In particular what is the boundary between being low, medium, and highly malignant.

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Claim 14 and 32 is indefinite because it is not clear what is “eliciting the in vivo engraftment of human hematopoietic cells” so as to allow the metes and bounds of the claim to be determined. Does the fusion protein increase engraftment?

5 Claim 15 is indefinite because it not clear what is meant by “protecting” the liver from hepatotoxic agents. How is the liver protected.

Claim 32 is indefinite because it is not clear how the chimeric protein is “used” in the preparation of a medicament. For example is the chimeric protein a part of the medicament or merely used in the preparation where it not a part of the final product.

10 Claims 10, 11 and 34-36 are rejected for depending upon an indefinite base (or intermediate) claim and fail to resolve the issues raised above.

Claim Rejection, 35 U.S.C. 112

15 6. Claims 1-15 and 32-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the chimeric sIL-6R/IL-6 chimera disclosed in SEQ ID NO:7, does not reasonably provide enablement for analogs thereof with no defined structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

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While the person of ordinary skill in the art would, in light of the specification be able to isolate make the sIL-6R/IL-6 chimera disclosed in SEQ ID NO:7 the specification nor prior art disclose which amino acid are critical for structure and function, and how mutation could effect the activity of the chimeric construct. A given amino acid will not by any means have the same

5 significance in different peptide sequences, or even in different positions of the same sequence. Therefore, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for functional chimeric protein, comprising sIL-6R/IL-6, would prevent the skilled artisan from determining whether any modification or mutation to the construct molecules could be made which retains the desired function of the instant invention,

10 because any random mutation or modification manifested within said protein itself would be predicted to adversely alter its biologically active 3-dimensional conformation, without undue experimentation to determine otherwise. Due to the large quantity of experimentation necessary to make fusion proteins with non immunogenic linker, the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said

15 fusion proteins, the unpredictability of the effects of mutation on the structure and function of proteins (since mutations of SEQ ID NO:7, are also encompassed by the claim), and the breadth of the claim which fail to recite specific functional limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope.

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Claim Rejections, 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

5 A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10 7. Claims 1 and 2 rejected under 35 U.S.C. 102(a) as being anticipated by Fischer (IDS ref. AH). Fisher et al disclose a fusion protein product of naturally-occurring sIL-6R and IL-6. The fusion product of Fisher is glycosylated in a similar fashion to the glycosylation of naturally-occurring sIL-6R and IL-6, as it is expressed in yeast, is essentially all of naturally-occurring sIL-
15 6R and IL-6 and also meets the definition of "analog" of sIL-6R/ IL-6, absent evidence to the contrary.

Advisory Information

20 Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

 If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

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Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi ^{ms}
Art Unit 1646
January 14, 2002

Michael D. Pak
MICHAEL PAK
PRIMARY EXAMINER